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Mini review

Microscopic hematuria in children☆

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ABSTRACT

The occurrence of microscopic hematuria (microhematuria) in children often causes concern for parents, patients, and physicians. The condition is usually benign in nature, so unnecessary laboratory tests should be avoided. A detailed history and physical examination must be undertaken, but a complete urinalysis with a microscopic examination is usually the only laboratory test required. The differential diagnosis of microhematuria is extensive, but the most important differentiating feature is the presence or absence of proteinuria. Urologists should ensure that serious conditions are not overlooked, unnecessary tests are not performed, and parents are properly reassured. However, there is still no consensus on the standard evaluation that should be used to determine microhematuria in children. The aim of this article is to provide a brief review of microhematuria in children and suggest a stepwise approach that can be used to detect major and/or treatable problems while avoiding unnecessary tests.

1. Introduction

Microscopic hematuria (microhematuria) is a worrisome clinical condition that usually prompts a patient to visit to a physician. Biannual mass urinary screenings of school children have been performed in Taiwan by the Chinese Foundation of Health since 1990.[1] As a result, many children with microhematuria are identified and referred to urologists on an annual basis.[2] Therefore, urologists must be familiar with the management of microhematuria in children. The major causes of microhematuria differ between children and adults, and the evaluation of this condition should reflect these differences. Renal disease is more common in children, while malignancies are more common in adults. The use of laboratory tests, radiological studies, and cystoscopy are well established for diagnosing adults, but the results are more variable in children. Follow-up examination for microhematuria after a negative evaluation is becoming less common in adults, but should remain as routine for diagnosing children.[3] This article provides a brief review of the signs and symptoms of microhematuria in children and proposes a stepwise approach for treating this medical condition.

2. Definition

Gross hematuria is visible to the naked eye, but microhematuria is typically detected by a dipstick via a reaction between peroxidase and hemoglobin. However, hematuria must be differentiated from pigmenturia, either hemoglobinuria or myoglobinuria, by microscopic examination of the urinary sediment.

Hematuria is defined by several parameters, the most common of which is the presence of 6 red blood cells (RBCs)/mL of urine in a counting chamber or 2 RBCs/high-power field (hpf) of urinary sediment.[4] There is still no consensus on the definition of microhematuria, although more than 5–10 RBCs/hpf is usually considered significant.[5,6] Some authors recommend that at least two of three urinalyses indicate microhematuria over a period of 2–3 weeks before performing further evaluations.[7,8]

3. Classification

In children with microhematuria, the presence or absence of clinical symptoms may help localize the source of the hematuria. For example, dysuria, changes in urinary frequency, enuresis, and bladder spasms suggest the presence of a lower urinary tract irritation (UTI). However, the signs and symptoms of glomerular disease may include edema, hypertension, abnormal creatinine levels, arthralgia, rashes, anemia, or hypoalbuminemia. Microhematuria may occur with or without proteinuria. Therefore, three categories of microhematuria have been proposed: (1) asymptomatic, isolated microhematuria, (2) asymptomatic microhematuria

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with proteinuria, and (3) microhematuria with clinical symptoms. In addition, microhematuria can be intermittent or persistent.

4. Incidence and prevalence

Depending on the definition used for making the diagnosis, the incidence and prevalence of microhematuria vary greatly in different reports. In school children, the incidence of microhematuria was estimated to be 0.41% when four urine specimens per child were collected; however, the incidence was 0.32% in girls and 0.14% in boys when five consecutive urine samples were analyzed over a period of 5 years. The prevalence of microhematuria among school children (6–15 years of age) is estimated to be 1–2%.[5,9] A screening program in Korea reported that the prevalence of microhematuria among 5 million schoolchildren is 0.8%.[10] In contrast, a screening study of 160,000 junior high children in Japan found that the prevalence of isolated microhematuria is as low as 0.15%.[11]

5. Pathophysiology

Hematuria may originate from the glomeruli, renal tubules, interstitium, or the urinary tract (including the collecting system, ureter, bladder, or urethra). Unlike adults, in children the source of bleeding is the glomeruli more often than the urinary tract. RBCs may cross the glomerular endothelial barrier and enter the capillary lumen through structural discontinuities in the capillary wall.[12] As with any form of glomerulonephritis, proteins, RBC casts, and deformed RBCs may accompany hematuria. In patients with hemoglobinopathy, or those who have been exposed to toxins, the renal papillae are susceptible to necrotic injury from microthrombi and anoxia. Transient episodes of microhematuria, or even gross hematuria, may occur during systemic infections or after moderate exercise in patients with renal parenchymal lesions. This may result from renal hemodynamic responses to exercise or fever via undetermined mechanisms.[13]

6. Differential diagnosis

There are various causes of microhematuria in children. The most common causes include benign familiar hematuria, hypercalciuria, immunoglobulin A (IgA) nephropathy, sickle cell traits, anemia, and complications due to a transplant. Less common causes include Alport's nephritis, post-infectious glomerulonephritis, trauma, exercise, renal stones, and Henoch-Schonlein purpura. Certain drugs and toxins (e.g., aspirin, sulfonamide, lead, etc.), coagulopathies, UTIs, tuberculosis, tumors, vascular malformations, structural anomalies, any form of glomerulonephritis, and lupus nephritis may occasionally cause microhematuria.[14]

Although the differential diagnosis for microhematuria is extensive, the most important differentiating feature is the presence or absence of proteinuria. Persons with significant proteinuria require rapid evaluation and early referral to a nephrologist. Those persons who do not have proteinuria should receive a follow-up examination and stepwise evaluation.[4]

7. Management

7.1. History

Changes inurinary frequency or urgency, dysuria, or flank pain may indicate a UTI. Transient hematuria may be associated with recent trauma, strenuous exercise, menstruation, or bladder catheterization. A history of a recent sore throat or skin infection suggests post-infectious glomerulonephritis. Exposure to certain drugs or toxins, including amitriptylene, anticoagulants, aspirin, chlorpromazine, ritonavir, indinavir, carbon monoxide, mushrooms, sulfonamide, tin compounds, lead, and/or phenol, may cause microhematuria. In addition, a family history of hematuria, hearing loss, hypertension, nephrolithiasis, renal diseases, renal cystic diseases, hemophilia, sickle cell traits, dialysis, and organ transplants should also be determined and evaluated.

7.2. Physical examination

The presence of elevated blood pressure usually indicates a more serious nephrological problem that requires further evaluation. UTIs are often accompanied by fever or costovertebral angle tenderness. A palpable abdominal mass suggests the presence of a tumor, hydronephrosis, multicystic dysplastic kidney, or polycystic kidney disease. Coexistence with rashes or arthritis suggests Henoch-Schonlein purpura and/or systemic lupus erythematosus. Edema is an important sign of nephrotic syndrome.

7.3. Laboratory tests

For a child suspected of having microhematuria, only two diagnostic tests are required. The first is a test for proteinuria that may indicate glomerulonephritis or nephrotic syndrome, and the second is a microscopic examination of the urine for RBC casts that may indicate a glomerular source of the hematuria. Phase-contrast microscopy and particle-size discrimination might be able to distinguish between glomerular and non-glomerular sources of hematuria. However, the identification of dysmorphic RBCs rarely offers additional information that is helpful in managing microhematuria.[15,16]

7.4. Indications for prompt evaluation

A prompt evaluation should be undertaken following the discovery of any of the following findings: hypertension, edema, oliguria, significant proteinuria ($>$ 500 mg/24 hours), or RBC casts in the urine. This evaluation should include a complete blood count (to diagnose hemolytic-uremic syndrome), throat culture, streptozyme panel, and determination the serum C3 concentration (to diagnose acute post-streptococcal glomerlonephritis) and serum creatinine and potassium concentrations (if renal insufficiency has been determined); 24-hour urine collection, in order to determine protein, creatinine, and calcium levels, should also be performed if the diagnosis remains unclear.[13] Referral to a pediatric nephrologist should be considered if the above evaluations suggest a potentially serious nephrological problem.

7.5. Imaging studies

Renal ultrasonography, as a noninvasive screening test, provides valuable information regarding the presence of stones, tumors, hydronephrosis, renal parenchymal dysplasia, structural anomalies, renal diseases, and bladder anomalies. Although the amount of information that can be provided by renal ultrasonography for the evaluation of microhematuria in children remains undetermined, the cost and time may be justified in terms of reassurance purposes.[17] Renal ultrasonography may be adequate for most children with microhematuria because the most common diagnoses include benign familial hematuria, idiopathic hypercalciuria, IgA nephropathy, and Alport's syndrome.[18] A more extensive evaluation is only required if proteinuria or other indicators are present. Other commonly used urological imaging studies, such as intravenous pyelography, voiding cystourethrography, renal nuclear scans, and cystoscopy, rarely yield useful information for the treatment of microhematuria and should not be routinely used for the evaluation of microhematuria in children.[13,17]

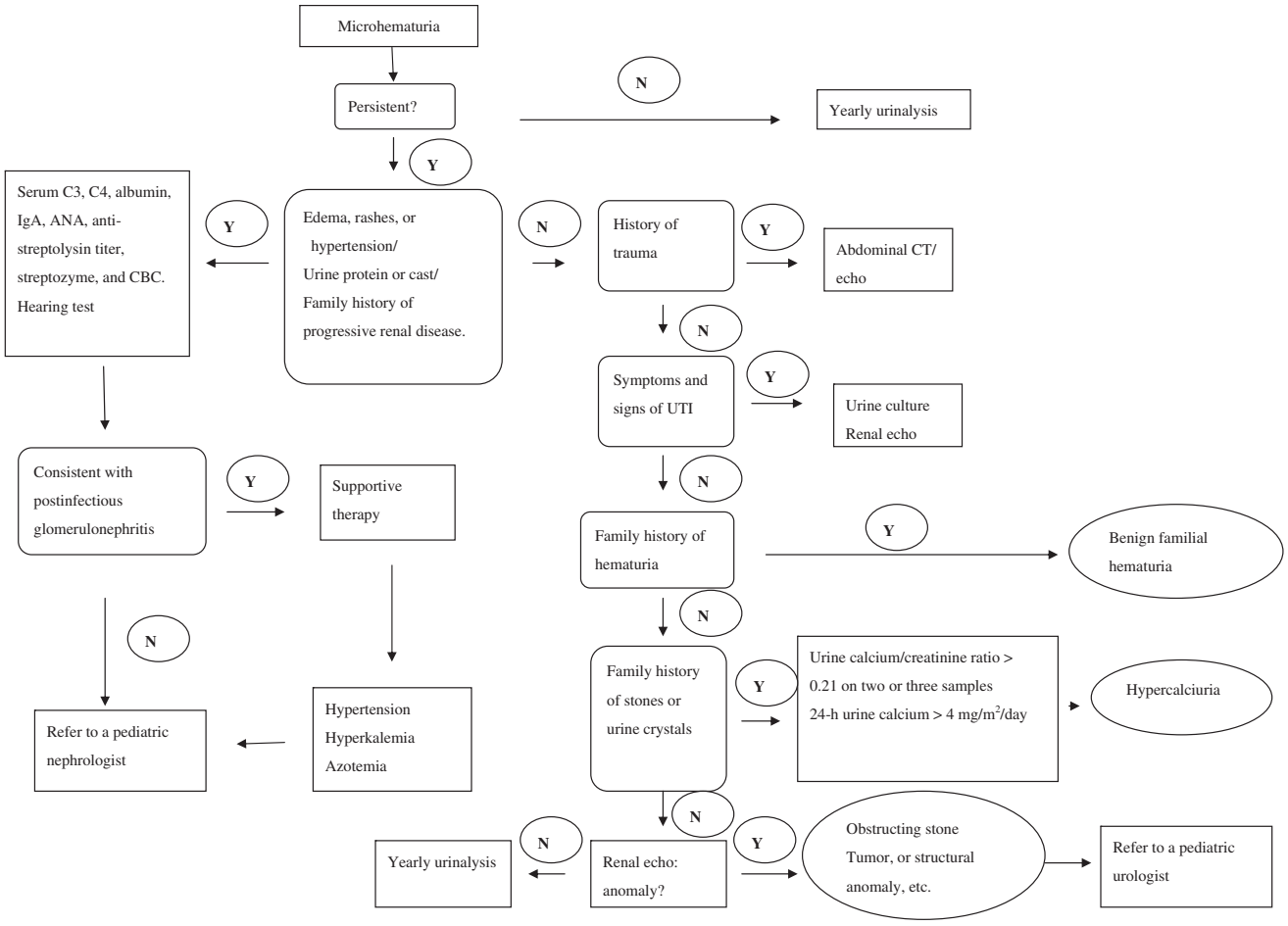

Figure 1. Algorithm for evaluating pediatric microscopic hematuria. ANA = antinuclear antibodies; CBC = complete blood count; CT = computed tomography; IgA = immunoglobulin A; N = no; Y = yes.

7.6. Renal biopsy

Renal biopsies rarely yield additional information that can be used to manage children with isolated microhematuria, except for those with documented episodes of gross hematuria or a close relative with a history of hematuria.[13] In a study of 155 children with isolated microhematuria (excluding non-glomerular causes of hematuria), renal biopsies revealed no clinically significant findings that required therapy. More than two-thirds of the biopsies indicated a thin basement membrane, Alport's syndrome, or IgA nephropathy, none of which have specific therapies. The remaining third of the biopsies indicated normal or insignificant findings.[19]

The algorithm for evaluating a child with microscopic hematuria is shown in Figure 1. If there are no indications that require immediate intervention after a stepwise evaluation, the parents should be reassured that there are no life-threatening problems, such as cancer, leukemia, or chronic kidney damage, and that most cases of isolated microhematuria in children do not warrant treatment; yearly urinalysis should be adequate for managing the patient's condition.[4] However, further evaluation is warranted if changes occur in the child's condition.

8. Conclusions

Microhematuria is prevalent in children and worrisome to parents and patients. Even though not all children require the same evaluations, a detailed history and physical examination must always be undertaken. A complete urinalysis with a microscopic examination is the only laboratory test that is uniformly required of these children. The remaining evaluations should be tailored according to the patient's medical history, physical examination, and abnormal findings on urinalysis. Most causes of microhematuria in children indicate medical conditions that usually require referral to a pediatric nephrologist. Indications that require referral to a urologist are less common, but include obstructing stones, renal injury from trauma, and anatomical anomalies.

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